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EXAMINER	
HELM, CARALYNNE E	
ART UNIT	PAPER NUMBER
1615	

NOTIFICATION DATE	DELIVERY MODE
05/13/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/742,346	FALOTICO ET AL.	
	Examiner	Art Unit	
	CARALYNNE HELM	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 March 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6-8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/30/10*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Note to Applicant: References to paragraphs in non-patent literature refer to full paragraphs (e.g. 'page 1 column 1 paragraph 1' refers to the first full paragraph on page 1 in column 1 of the reference)

Election/Restrictions

To summarize the current election, applicants elected group I, without traverse.

NEW REJECTIONS/OBJECTIONS

Claim Objections

Claim 6 is objected to because of the following informalities: the claim appears to omit 'trichostatin A" between the recitation "elution rate of the" and the recitation "and the rapamycin" in the last line on page 2 of the claims. In addition, "polyvinyledenefluoride" is a misspelling of "polyvinylidenefluoride" and "hexafluropropylene" is a misspelling of "hexafluoropropylene". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 6-8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was

not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The recitation "from solution to create a phase separation of two distinct layers" was not a concept or recitation that appeared in the disclosure as originally filed. Therefore this constitutes new matter.

Claims 6-8 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the medical device with basecoat composed of trichostatin A and rapamycin with 60/40 weight ratio of vinylidenefluoride-co-hexafluoropropylene along with a topcoat of poly(n-butyl methacrylate), does not reasonably provide enablement for claim product made by the recited product-by-process wherein the basecoat and topcoat are mixed and precipitated from solution to create a phase separation of two distinct layers. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. The preparation of the bi-layered system via phase separation of an immiscible polymer blend from solution is not taught. In addition, Ton-That et al. (Polymer 200142:1121-1129) discuss the wide variation and unpredictability in phase morphology for solution cast immiscible blends (see page 1121column 2 paragraph 1). Here depending on the solvent used on, different polymers in a binary blend can dominate the surface of the blend. In addition, the proportion of polymer sin the blend as well as the rate of solvent evaporation also has a marked effect of the phase morphology (see page 1121 column 1 paragraph 1).

Moreover in the instant case, there is the complicating factor of the locale of the two incorporated drugs relative to the segregated phases. Since applicants provided no guidance as to steps necessary to start with a solution of the two polymers and end with the bi-layered, phase separated, drug containing claimed structure, one of ordinary skill in the art would not be enabled to generate the claimed device via the recited product-by-process in a predictable fashion.

MAINTAINED REJECTIONS

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

The four factual inquiries of Graham v. John Deere Co. have been fully considered and

analyzed in the rejections that follow.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 6-7 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Tseng et al. (previously cited) in light of Windecker et al. (previously cited) and Roorda et al. (previously cited).

In claim 1, Tseng et al. teach a stent (an implantable structure), containing drug depots capable of controllably delivering one or more histone deacetylase (HDAC) inhibitors (see instant claims 6-7). In addition, Tseng et al. also teach that the disclosed device delivering the HDAC inhibitors is particularly beneficial in the treatment of restenosis, implying that the HDAC inhibitors would be present at therapeutic dosages within the stent device (see paragraph 37; instant claim 6). Tseng et al. go on to further describe the HDAC inhibitor included on or in the stent body as trichostatin A, abbreviated as TSA (see claims 12-14 and paragraph 15 lines 1-2; instant claim 9). Tseng et al. teach the effectiveness of TSA at 50 nano molar in the inhibition of smooth muscle cell proliferation (see paragraph 168; instant claim 6). Also taught by Tseng et

al. is the inclusion of an additional pharmaceutical agent or agents, such as anti-inflammatory and anti-proliferative agents, where an exemplary agent includes rapamycin as a preferred option (see paragraph 134 and claims 2 and 3; instant claim 6). Further, Tseng et al. teach that the drug depots include one or more polymers (see claim 6). Tseng et al. does not specifically describe the polymer-drug configuration as a coating on the stent device.

Windecker et al. teach that rapamycin (also known as sirolimus) has powerful anti-proliferative and anti-migratory drug properties on vascular smooth muscle cells (see page 1089 column 1 paragraph 1 lines 1-5; instant claim 10). In addition, Windecker et al. go on to teach that its incorporation into biocompatible polymers, suitable for stent based drug delivery, has been successful (see page 1089 column 1 paragraph 1 lines 5-7; instant claim 10). Further, this drug is utilized for the treatment of restenosis.

Roorda et al. teach a drug eluting stent with drug-polymer base layer and an additional polymer topcoat (see paragraph 12 lines 1-4; instant claim 6). Roorda et al. go on to teach that the topcoat serves as a rate limiting membrane to control the release of drug from the device (see paragraph 12 lines 8-11; instant claim 6). Roorda et al. teach that these coating layers are composed of polymers and that both polyacrylates alone and in conjunction with fluorinated polymers are considered suitable varieties (see paragraph 28 and 29 lines 1-3; instant claim 6). Further, Roorda et al. teach a configuration where poly(n-butyl methacrylate) is used as a topcoat and in a blend with another polymer in the drug containing layer (see paragraph 29 and example 18). One

such other polymer is taught to be a fluorinated polymer, namely poly(vinylidene fluoride-co-hexafluoro propene) (see paragraph 28). This copolymer is exemplified in use as a coating on the device where the proportion of vinyldiene fluoride to hexafluoro propene is 85:15 (see example 12). Differing polymer properties and associated drug release kinetics are achieved as the proportion of the monomer in the polymer backbone of the coating is varied. Various amounts of poly(n-butyl methacrylate) are taught to be included in the topcoat including 200 μg and 300 μg. Since the amount of polymer present in the topcoat has a controlling effect on the rate of release of the contained drug, it would have been obvious to one of ordinary skill in the art to optimize this quantity to achieve particularly desired release kinetics. The reference does not teach the particular claimed vinyldiene fluoride to hexafluoro propene ratio in the copolymer or amount of poly(n-butylmethacrylate) present in the topcoat. However, at the time of the claimed invention, it would have been well within the purview of one of ordinary skill in the art to optimize such parameters as a matter of routine experimentation and achieve the claimed values.

One of ordinary skill in the art at the time of the invention would have found it obvious to couple the device of Tseng et al. with the teachings of Windecker et al. to produce a stent (an implantable medical device) containing drug depots capable of controllably releasing therapeutic dosages of trichostatin A and rapamycin, an anti-proliferative. In addition, since both Roorda and Tseng et al. teach stents with polymeric matrices that provide for controllable release of a combination of drugs to address restenosis, one of ordinary skill in the art at the time of the invention would

have found it obvious to utilize the particular polymers and layer configuration as taught by Roorda et al. in the invention of Tseng et al. in view of Windecker et al. Instant claim 6 recites a product-by-process. "'[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process.' In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985)....The structure implied by the process steps should be considered when assessing the patentability of product-by-process claims over the prior art, especially where the product can only be defined by the process steps by which the product is made, or where the manufacturing process steps would be expected to impart distinctive structural characteristics to the final product. See, e.g., In re Garnero, 412 F.2d 276, 279, 162 USPQ 221, 223 (CCPA 1979)" (see MPEP 2113). Therefore when no structure is implied, the product-by-process recitation does not add any limitations that affect patentability. There is no additional structure defined by the process steps, therefore the product-by-process recitation does not add any limitations that affect patentability. Applicant teaches in the instant specification that any combination of fluoropolymer and acrylics would produce incompatible polymer chemistry, therefore the described coating formulations of Roorda et al. would have the claimed characteristic of immiscibility (see instant specification page 127 lines 11-15 and claim 6). Since all three inventions address the issue of the body's response to medical device

implantation (drug eluting stents) one skilled in the art would have had a reasonable expectation of success for the combination. Furthermore, applicant teaches that the shear presence of rapamycin (sirolimus) with trichostatin A may potentiate each other's anti-restenotic activity (see instant specification page 9 lines 21-25). According to MPEP 2112.01, "A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present." This treatment results from In re Spada, which states that, "Products of identical chemical composition can not have mutually exclusive properties." In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Since Tseng et al. in view of Windecker et al. and Roorda et al. make obvious the claimed device with trichostatin A and rapamycin present in combination, it also would have this potentiation effect between the two actives. Thus, claims 6-7 are obvious over Tseng et al. in view of Windecker et al. and Roorda et al.

Claims 6 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tseng et al. in light of Windecker et al. and Roorda et al. as applied to claims 6 and 7 above, and further in view of Carter et al. (previously cited).

As previously described Tseng et al. modified by both Windecker et al. and Roorda et al. teach a stent device with drug depots containing trichostatin A and rapamycin, where the claimed drugs at the claimed concentration are contained within a polymeric basecoat and are able to be controllably released in therapeutic dosages, and further contains a polymeric topcoat that controls the drug elution and whose polymer is

immiscible with that of the basecoat (see above). The modified Tseng et al. reference also teaches that the reason for incorporating the trichostatin A within the stent device is for dealing with the issue of restenosis following stent implantation (see Tseng et al. paragraphs 29, 31, and 37). Tseng et al. modified by Windecker et al. and Roorda et al. does not specifically teach stent grafts containing the drug depots with controllable release capabilities.

Carter et al. teach that stents are commonly used to clear obstructions and to repair damage to vascular tissue (see paragraph 39 lines 2-5). Carter et al. go on to teach that stent grafts are a common name for a modification of stents where a flexible covering is attached to the stent frame (see paragraph 39 lines 10-12) and that the implantation process for stents, as a whole, carries with it the risk of causing restenosis (see paragraph 50 line 9). Since stent grafts are a modification of stents and also subject to post-implantation restenosis, it would have been obvious to one skilled in the art at the time of the invention to further modify the invention of Tseng et al. in light of Windecker et al. and Roorda et al., by incorporating the controllably releasing drug depots, configured as a bilayered polymeric coating containing trichostatin A at about 40 nano molar and rapamycin, within a stent-graft device. Therefore, instant claims 6 and 8 are obvious over Tseng et al. in light of Windecker et al., Roorda et al., and Carter et al.

Response to Arguments

Applicants' arguments, filed March 25, 2010, have been fully considered but they are not deemed to be persuasive.

Applicants argue that the cited combination of references does not teach the claimed limitations. Specifically, applicants point out that Roorda et al. teach polymer blends in their layers and that this is different from the instant invention. The instant claims do not exclude the presence of additional polymers from either of the taught layers. Since the combination of references teaches or makes obvious the recited devices with their 60/40 vinylidenefluoride-co-hexafluoropropylene, rapamycin and trichostatin A containing base coat and poly(n-butyl methacrylate) topcoat, the claims are rendered obvious. Moreover, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The rejections and/or objections detailed above are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CARALYNNE HELM whose telephone number is (571)270-3506. The examiner can normally be reached on Monday through Friday 9-5 (EDT).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert A. Wax can be reached on 571-272-0623. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Caralynne Helm/
Examiner, Art Unit 1615

/S. TRAN/
Primary Examiner, Art Unit 1615